

of a link between UK products containing phenylpropranolamine and haemorrhagic stroke was weak (phenylpropranolamine is not licensed as an appetite suppressant in the UK and the maximum recommended dose of 100 mg daily was lower than the 150 mg daily recommended in the USA). It was therefore suggested by UK commentators that use of licensed doses, with appropriate precautions, posed no additional risk.² However, subsequently, UK preparations containing phenylpropranolamine have either been reformulated (mainly with pseudoephedrine) or withdrawn by the manufacturers.

1. Lake CR, et al. Adverse drug effects attributed to phenylpropranolamine: a review of 142 case reports. *Am J Med* 1990; **89**: 195–208.
2. Moffatt T, et al. Phenylpropranolamine: putting the record straight. *Pharm J* 2000; **265**: 817.
3. Kernan WN, et al. Phenylpropranolamine and the risk of hemorrhagic stroke. *N Engl J Med* 2000; **343**: 1826–32.
4. Ernst ME, Hartz A. Phenylpropranolamine and hemorrhagic stroke. *N Engl J Med* 2001; **344**: 1094.
5. Wolowich WR, et al. Phenylpropranolamine and hemorrhagic stroke. *N Engl J Med* 2001; **344**: 1094–5.
6. Stier BG, Hennekens CH. Phenylpropranolamine and hemorrhagic stroke in the Hemorrhagic Stroke Project: a reappraisal in the context of science, the Food and Drug Administration, and the law. *Ann Epidemiol* 2006; **16**: 49–52.
7. Committee on Safety of Medicines/Medicines Control Agency. Phenylpropranolamine and haemorrhagic stroke. *Current Problems* 2001; **27**: 5–6. Also available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON007458&RevisionSelectionMethod=LatestReleased (accessed 04/01/07)

Interactions

As for Sympathomimetics, p.1407. For a comment that drug interactions were likely to have been involved in many adverse events associated with phenylpropranolamine see under Adverse Effects and Precautions, above. Due to its indirect action, hypertensive crisis is a particular risk in patients receiving MAOIs.

Amantadine. Severe psychosis has been reported¹ in a woman taking amantadine with phenylpropranolamine. In another report,² a 39-year-old man had intense and recurrent *déjà vu* experiences after taking amantadine with phenylpropranolamine for viral influenza. The effect ceased when he stopped both drugs. The authors suggested that his symptoms were due to increased dopamine activity caused by the combination.

1. Stroe AE, et al. Psychotic episode related to phenylpropranolamine and amantadine in a healthy female. *Gen Hosp Psychiatry* 1995; **17**: 457–8.
2. Taiminen T, Jääskeläinen SK. Intense and recurrent *déjà vu* experiences related to amantadine and phenylpropranolamine in a healthy male. *J Clin Neurosci* 2001; **8**: 460–2.

Antipsychotics. A 27-year-old woman with schizophrenia and T-wave abnormality of the heart, who had responded to *thioridazine* 100 mg daily with procyclidine 2.5 mg twice daily, died from ventricular fibrillation within 2 hours of taking a single dose of a preparation reported to contain chlorphenamine maleate 4 mg with phenylpropranolamine hydrochloride 50 mg (*Contact C*), concurrently with thioridazine.¹

1. Chouinard G, et al. Death attributed to ventricular arrhythmia induced by thioridazine in combination with a single *Contact C* capsule. *Can Med Assoc J* 1978; **119**: 729–31.

Antivirals. A patient taking an over-the-counter nasal decongestant preparation containing phenylpropranolamine and clemastine as well as a triple-drug HIV prophylactic regimen, had a hypertensive crisis 3 days after *stavudine* was substituted for *zidovudine*¹; the other antivirals in the regimen were *indinavir* and *lamivudine*.

1. Khurana V, et al. Hypertensive crisis secondary to phenylpropranolamine interacting with triple-drug therapy for HIV prophylaxis. *Am J Med* 1999; **106**: 118–19.

Bromocriptine. For a report of hypertension and life-threatening complications after use of phenylpropranolamine with bromocriptine, see Sympathomimetics, p.800.

NSAIDs. A 27-year-old woman who had been taking *D*-phenylpropranolamine [sic] 85 mg daily for some months, experienced severe hypertension when she also took *indometacin* 25 mg. It was considered that the inhibition of prostaglandin synthesis by *indometacin* might have caused enhancement of the sympathomimetic effect of phenylpropranolamine.¹

1. Lee KY, et al. Severe hypertension after ingestion of an appetite suppressant (phenylpropranolamine) with *indometacin*. *Lancet* 1979; **i**: 1110–11.

Pharmacokinetics

Phenylpropranolamine is readily and completely absorbed from the gastrointestinal tract, peak plasma concentrations being achieved about 1 or 2 hours after oral doses. It undergoes some metabolism in the liver, to an active hydroxylated metabolite, but up to 80 to

90% of a dose is excreted unchanged in the urine within 24 hours. The half-life has been reported to be about 3 to 5 hours.

References

1. Simons FER, et al. Pharmacokinetics of the orally administered decongestants pseudoephedrine and phenylpropranolamine in children. *J Pediatr* 1996; **129**: 729–34.
2. Chester N, et al. Elimination of ephedrine in urine following multiple dosing: the consequences for athletes, in relation to doping control. *Br J Clin Pharmacol* 2004; **57**: 62–7.

Uses and Administration

Phenylpropranolamine is a mainly indirect-acting sympathomimetic (p.1408) with an action similar to that of ephedrine (p.1559) but less active as a CNS stimulant.

Phenylpropranolamine has been given orally as the hydrochloride for the symptomatic treatment of **nasal congestion** (p.1548). It has frequently been used in combination preparations for the relief of cough and cold symptoms.

In the management of nasal congestion, phenylpropranolamine hydrochloride has been given in oral doses of up to 50 mg twice daily as modified-release preparations.

Other uses of phenylpropranolamine have included the control of urinary incontinence in some patients (see p.2180). It has also been given in the management of some forms of priapism (see under Metaraminol, p.1333). Phenylpropranolamine has been used to suppress appetite in the management of obesity (p.2149) but the use of stimulants is no longer recommended.

Phenylpropranolamine polistirex (a phenylpropranolamine and sulfonated diethylenbenzene-ethylenbenzene copolymer complex) has also been used, as have phenylpropranolamine bitartrate, phenylpropranolamine maleate, and phenylpropranolamine sulfate.

Preparations

USP 31: Chlorpheniramine Maleate and Phenylpropranolamine Hydrochloride Extended-release Capsules; Chlorpheniramine Maleate and Phenylpropranolamine Hydrochloride Extended-release Tablets; Phenylpropranolamine Hydrochloride Capsules; Phenylpropranolamine Hydrochloride Extended-release Capsules; Phenylpropranolamine Hydrochloride Extended-release Tablets; Phenylpropranolamine Hydrochloride Oral Solution; Phenylpropranolamine Hydrochloride Tablets.

Proprietary Preparations (details are given in Part 3)

Fin.: Rinexin; **Ger.:** Boxogetten S; Recatal mono; **Norw.:** Rinexin; **Philipp.:** Decolgen; Desotap; Disudrin; Naldec; Nasadec; Nasaphen; Nasatera P; Neo-Coldan; **S.Afr.:** Restaslim†; **Swed.:** Rinexin; **Switz.:** Kontexin†; Merex†; Slim Caps.

Multi-ingredient: numerous preparations are listed in Part 3.

Pholcodine (BAN, rINN)

Folcodina; Folkodiini; Folkodin; Folkodin monohydrát; Folkodinas; Pholcodinum; Pholcodinum Monohydricum. 3-O-(2-Morpholinoethyl)morphine monohydrate.

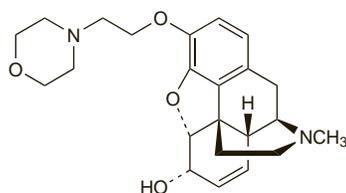
ФОЛКОДИН

$C_{23}H_{30}N_2O_4 \cdot H_2O = 416.5$.

CAS — 509-67-1 (anhydrous pholcodine).

ATC — R05DA08.

ATC Vet — QR05DA08.



Pharmacopoeias. In *Chin.* and *Eur.* (see p.vii).

Ph. Eur. 6.2 (Pholcodine). A white or almost white crystalline powder or colourless crystals. Sparingly soluble in water; freely soluble in alcohol and in acetone; dissolves in dilute mineral acids.

Adverse Effects and Precautions

As for Dextromethorphan, p.1555. Constipation, drowsiness, and skin rashes have been reported occasionally.

Interactions

Use of pholcodine with alcohol or other CNS depressants may increase the effects on the CNS.

Uses and Administration

Pholcodine is a centrally acting cough suppressant that has actions and uses similar to those of dextromethorphan (p.1556). It is given orally in a usual dose of 5 to 10 mg three or four times daily. For children's doses, see Administration in Children, below. The citrate has also been used. Pholcodine polistirex (a pholcodine and sulfonated diethylenbenzene-ethylenbenzene copolymer complex) has been used in modified-release preparations.

Administration in children. Although pholcodine is licensed for use in children, over-the-counter cough and cold preparations containing cough suppressants (including pholcodine) should be used with caution and generally avoided in those under 2 years of age (see p.1547). The following oral doses of pholcodine are given in the *BNFC* for use in children:

- 2 to 5 years: 2 mg three times daily
- 5 to 12 years: 2 to 5 mg three or four times daily

Preparations

BP 2008: Pholcodine Linctus; Strong Pholcodine Linctus.

Proprietary Preparations (details are given in Part 3)

Austral.: Actified CC Dry†; Actuss†; Duro-Tuss; Logicin Cough Suppressant†; Nyal Plus† Dry Cough†; Ordov Dry Tickle Cough†; Pholtrate†; Tussinol; **Cz.:** Neocodinj; **Fin.:** Tuxi; **Fr.:** Biocalyptol; Broncorinol toux sèche†; Codotussyl Toux Seche; Dimetane; Humex; Pharmakod toux sèche; Respitene; Rhinathiol Toux Seche Pholcodine; Sirop des Vosges Toux Seche; **Hong Kong:** Duro-Tuss; Uni-Pholco; **Ind.:** Expulin Dry Cough; Pholcodex; Pholcolin; **Malaysia:** Dhacodine; Duro-Tuss; **Norw.:** Tuxi; **NZ:** Actified CC Dry†; Duro-Tuss; **S.Afr.:** Pholcolint; Pholtec; **Singapore:** Duro-Tuss; **Spain:** Trophires†; **UK:** Berylin Childrens Dry Coughs; Boots Dry Cough Syrup 1 Year Plus; Galenphol; Hill's Balsam Dry Cough; Pavacol-D; Tixilyx Daytime.

Multi-ingredient: **Austral.:** Chemists Own Kiddico; Demazin Cough & Cold; Diffiam Anti-inflammatory Lozenges with Cough Suppressant; Duro-Tuss Cough Lozenges; Duro-Tuss Decongestant; Duro-Tuss Dry Cough Plus Nasal Decongestant; Duro-Tuss Expectorant; Phensedyl†; Tixilyx Night-time; **Belg.:** Broncho-pectorals Pholcodine; Eucalyptine Pholcodine; Eucalyptine Pholcodine Le Brun†; Folex†; Norhitis; Pectorhiny†; Pholco-Merprine; **Cz.:** Biocalyptol S†; **Fr.:** Atoux; Broncalene; Clarix; Denoral†; Hexapneumine; Isomyrtine†; Polery; Trophires; **Hong Kong:** Biocalyptol†; Duro-Tuss Decongestant; Duro-Tuss Expectorant; Hexapneumine; Tripe P; **India:** Tixilyx; **Ind.:** Day Nurse; Expulin; Expulin Childrens Cough; **Malaysia:** Diffiam Anti-inflammatory Lozenges (with cough suppressant); Duro-Tuss Expectorant; Phensedyl Dry Cough; Promedy† Plus; Rhynacol; Russedyl Plus; Tixilyx†; **NZ:** Diffiam Cough; Duro-Tuss Cough; Duro-Tuss Expectorant; Duro-Tuss Lozenges; Phensedyl Dry Family Cough†; Tixilyx; **S.Afr.:** Contra-Coff; Docsed; Folcofen; Pholtec Linctus; Procof; Respinol Compound; Tixilyx; **Singapore:** 3P†; Duro-Tuss Cough Lozenges; Duro-Tuss Decongestant; Duro-Tuss Expectorant; **Spain:** Caltoson Balsamico; **Switz.:** Pecto-Baby; Phol-Tussil; Phol-Tux; Tussiplex†; **UK:** Boots Nighttime Cough Syrup 1 Year Plus; Cough Nurse; Day & Night Nurse; Day Nurse; Expulin Childrens Cough†; Nirolex Day Cold & Flu; Nirolex Night Cold & Flu; Tixilyx Cough & Cold; Tixilyx Night-Time.

Pipazetate (BAN, rINN)

D-254; Pipazétate; Pipazetato; Pipazetato; Pipazethate (USAN); SKF-70230-A; SQ-15874. 2-(2-Piperidinoethoxy)ethyl pyrido[3,2-b][1,4]benzothiazine-10-carboxylate.

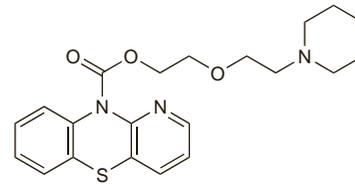
Пипазетат

$C_{21}H_{25}N_3O_3S = 399.5$.

CAS — 2167-85-3.

ATC — R05DB11.

ATC Vet — QR05DB11.



Pipazetate Hydrochloride (BANM, rINNM)

Hydrocloruro de pipazetato; Pipazétate, Chlorhydrate de; Pipazetati Hydrochloridum; Pipazethate Hydrochloride; Piperestazine Hydrochloride.

Пипазетата Гидрохлорид

$C_{21}H_{25}N_3O_3S \cdot HCl = 436.0$.

CAS — 6056-11-7.

ATC — R05DB11.

ATC Vet — QR05DB11.